REMARKS

Status of the Claims

Claim 20 is canceled. Claim 1 is amended to clarify the class of symptoms being treated; further amendments to claim 1 are editorial in nature. Dependency is amended in claims 2, 5 and 8 to include new claims 22 and 23, which respectively recite each of the individual alternative symptom classes recited in claim 1.

No new matter has been added.

Anticipation by Saji

Claims 1, 2, 5, 8, 11 and 20 are rejected under 35 USC § 102(b) as anticipated by Saji et al. EP '846. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that Saji EP '846 teaches treatment of schizophrenia by administration of the claimed compound with a daily dose, for an adult, of from 1 to 1000 mg, or from 0.1 to 100 mg if administered orally.

Saji EP '846 does **not** anticipate the present invention. The present claim 1 recites treatment of two particular classes of symptoms of the particular disease (schizophrenia) by administration of a particular compound (Lurasidone or its salts).

On the other hand, as explained in previous responses, Saji EP '846 describes the compound very broadly (see, formula I at p. 4) and names specifically at least 200 compounds that are to be used for "antipsychotic" treatments broadly stated (p. 3, lines 3-4). Nowhere in Saji EP '846 is the particular compound recited in the present claim 1 (Lurasidone) associated with effective treatment of schizophrenia particularly, and especially there is no association of Lurasidone with the treatment of negative symptoms of schizophrenia or with the treatment of cognitive dysfunction arising from schizophrenia.

Furthermore, there is no indication in Saji EP '846 that Lurasidone is effective in treating these symptoms without inducing any extrapyramidal symptoms. There is not any recognition by Saji EP '846 that "negative symptoms" are something that should be addressed in an effective treatment of schizophrenia nor that extrapyramidal symptoms are to be avoided.

It is well-established that a broad, generic teaching is not anticipatory of a claim directed to a particular combination of elements in the absence of direction within the reference toward that combination. See, *In re Petering* 133 USPQ 275 (CCPA 1962). Saji EP '846 does not provide any such direction as explained above, and so does not anticipate the present invention.

Anticipation also requires that each and every feature of the claim be described in the reference. As explained above, Saji EP '846 fails to disclose at least one feature in the present claim 1, and so fails to anticipate claim 1 or the claims dependent therefrom. The instant rejection must be withdrawn for this second reason as well.

Obviousness

Claims 1, 2, 5, 8, 11 and 20 are rejected under 35 USC § 103(a) as obvious over Saji EP '846. Claims 1, 2, 5, 8, 11 and 20 are also rejected under 35 USC § 103(a) as obvious over Sommerville WO '039 in view of Wong '962 alone or in view of Saji EP '846. These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that the references teach the treatment of schizophrenia by the claimed compound with the claimed dosage, particularly…

> "Sommerville et al. further teaches positive and negative symptoms are often increased during the acute phase, or the florid psychotic phase, of schizophrenia ..." (the Office Action, page 5, second paragraph), and
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> "There is nothing in Saji's reference which describes that negative symptoms were still prevailing while treating schizophrenia with the claimed compound." (the Office Action, page 7, third paragraph).

It is true that it has been known that negative symptoms are included in the symptoms of schizophrenia. However, it has been considered before filing of the present application that the known drugs for treatment of schizophrenia are effective for the treatment of positive symptoms of schizophrenia but not sufficiently effective for the treatment of negative symptoms of schizophrenia. At the time the present application was filed, there was no drug sufficiently effective for the treatment of negative symptoms of schizophrenia. This long-felt need in the art

is reflected in many publications. The following five papers are provided attached as exemplary:

Reference 1: Stephen M. Erhart et al., "Treatment of Schizophrenia Negative Symptoms: Future Prospects", Schizophrenia Bulletin, vol. 32, no. 2, pp. 234-237, 2006

Reference 2: Thomas Laughren et al., "Food and Drug Administration Perspective on Negative Symptoms in Schizophrenia as a Target for a Drug Treatment Claim", Schizophrenia Bulletin, vol. 32, no. 2, pp. 220-222, 2006

Reference 3: Larry Alphs, "An Industry Perspective on NIMH Congress Statement on Negative Symptoms", Schizophrenia Bulletin, vol. 32, no. 2, pp. 225-230, 2006

Reference 4: John Kane, "Commentary: Consensus Statement on Negative Symptoms", Schizophrenia Bulletin, vol. 32, no. 2, pp. 223-224, 2006

Reference 5: Brian Kirkpatrick et al., "The NIMH-MATRICS Consensus Statement on Negative Symptoms", Schizophrenia Bulletin, vol. 32, no. 2, pp. 214-219, 2006

Although published post-filing of the present application, these papers show that, even a few years after the priority date, the art of treatment of schizophrenia did not include any approved treatment that addressed negative symptoms of the disease. As mentioned in the Abstract and/or introductory passages of these papers, finding an agent effective for the treatment of negative symptoms of schizophrenia has been the object of a great deal of research effort, but the available drugs for schizophrenia do not exhibit sufficient effect upon the treatment of negative symptoms in schizophrenia.

The Examiner might note that Laughren et al. suggest that negative symptoms of schizophrenia might represent a completely different target for drug development from the positive symptoms of the disease. Alphs states in his abstract that, "Negative symptoms of schizophrenia remain an area of substantial unmet clinical need." The Examiner should take due note that failure of others to solve a problem and the solving of a long-felt need are two of

several secondary considerations deemed by the Supreme Court to be strong evidence of unobviousness of an invention.

> In *Graham* v. *John Deere Co. of Kansas City*, 383 U.S. 1 [148 USPQ 459] (1966), the Court set out a framework for applying the statutory language of §103, language itself based on the logic of the earlier decision in *Hotchkiss* v. *Greenwood*, 11 How. 248 (1851), and its progeny. See 383 U.S., at 15–17. The analysis is objective:
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> "Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *Id.*, at 17–18.

KSR v. Teleflex 82 USPQ2d 1385 (2007) at p. 1391.

Following intensive study, the present inventors found that lurasidone shows the desired effects on negative symptoms in schizophrenia. The effects of the compound of the present invention have been publicized at a meeting; the poster presenting these results is provided attached:

Reference 6: A poster exhibited at the 18th European College of Neuropsychopharmacology Congress, Amsterdam, Netherlands, October 22-26, 2005.

Fig. 2 of the poster shows the PANSS (= positive and negative syndrome scale) scores for the compound of the present invention. Lurasidone showed significantly higher effectiveness on the negative symptoms of schizophrenia in comparison with placebo in a clinical study. The poster further indicates that ...

A once-a-day dose of 40, 80 or 120 mg Lurasidone achieved clinically meaningful improvements across broad efficacy measures during 6-weeks of treatment, compared with placebo in acutely exacerbated schizophrenic patients.

Lurasidone improved positive and negative symptoms of schizophrenia, with significant effects first appearing three days after the initiation of treatment. The improvement in negative symptoms seen in Lurasidone treated patients may be related to the minimal sedative effects and low EPS profile of this drug, as a first demonstration of Lurasidone's possible cognitive benefit there was a significant improvement in the PANSS-cognitive component, combined with a favorable profile of minimal sedation.

The tolerability of Lurasidone appears quite favorable with no notable effects on lipid profile or glucose regulation or weight gain, suggesting Lursidone may have a favorable safety profile regarding cardiovascular events and diabetes. Overall, Lurasidone demonstrated a well-balanced profile of effectiveness and safety in patients with acute schizophrenia.

Further study will be needed to confirm this initial favorable profile.

Thus, Lurasidone was shown to be the first effective treatment for negative symptoms of schizophrenia and furthermore was also effective in treating the cognitive dysfunction of schizophrenia as well. Given the failure of previous treatments available in the art to address these two classes of symptoms and to do so without also causing undesirable extrapyramidal symptoms (sedation) these results must be considered unexpected by those of ordinary skill in the art (*e.g.*, as established by the five references attached hereto). Furthermore, these results represent a solution to a problem that many others have failed to solve, and furthermore solve a long-felt need in the art of treatment of schizophrenia. As pointed out above, this is substantial, objective evidence of unobviousness of the present invention.

The present inventors have also newly found that Lurasidone is also effective to treat cognitive dysfunction of schizophrenia, as is also proved by the clinical study reported in the poster Reference 6. The Examiner should again note Fig. 2 showing the PANSS in cognitive function: Lurasidone showed significantly higher effectiveness upon cognitive dysfunction of schizophrenia in comparison with a placebo in the clinical study.

As is explained above, at the time of filing of the present application, indeed to date, there are no approved drugs for treating schizophrenia that are effective on the negative symptoms of schizophrenia and upon cognitive dysfunction of schizophrenia, and especially none that also do not cause undesireable extrapyramidal symptoms. On the other hand, according to the intensive studies of the present inventors it has newly been found that the specific compound recited in the present claims, Lurasidone, can show significant effects on the negative symptoms of schizophrenia in addition to effects on the positive symptoms of schizophrenia, and further can also show significant effects on the cognitive dysfunction of schizophrenia. No known treatment for schizophrenia has been effective in treating all three classes of schizophrenia symptoms, and especially not without also causing undesired extrapyramidal symptoms.

Accordingly, the present invention as claimed is not disclosed or even suggested by any of Saji EP '846, Sommerville WO '039 or Wong '962, or any combination thereof. Thus, the present claims are not *prima facie* obvious over these references. Furthermore, the clinical results shown in the attached reference 6, showing that administration of Lurasidone solves a need long-felt in the art and a problem long unsolved, provide objective evidence of unobviousness of the present invention. Thus, the instant rejections of claims 1, 2, 5, 8, 11 and 20 (and if applied to 22 and 23) for obviousness must be withdrawn.

Applicants submit that the present invention is patentable over the prior art of record. The favorable actions of withdrawal of the standing rejections and allowance of the present claims are requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Registration

No. 36,623, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of $1,110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: December 10, 2009

Respectfully submitted,

By /Mark J. Nuell/
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Attachments: References 1-6
Stephen M. Erhart et al.
Thomas Laughren et al.
Larry Alphs
John Kane
Brian Kirkpatrick et al.
poster exhibited at the 18th European College of Neuropsychopharmacology Congress